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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JOYCE, CATHERINE	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,036	WOOD ET AL.	
	Examiner	Art Unit	
	Catherine M. Joyce	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 60-77* is/are pending in the application.

4a) Of the above claim(s) *1 and 69-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-68 and 74-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 1 and 60-77 are pending, and claims 1 and 66, 69-73 are withdrawn from consideration as being drawn to a non-elected invention.

2. Claims 60-65, 67-68 and 74-77 are under examination.

3. It is noted for applicant's convenience that the priority date for the instant application has been set at June 19, 2003, the filing date of the instant application. A review of parent case serial number 09/428156 does not reveal support for the claimed invention. If applicant disagrees with any rejection set forth in this office action based on examiner's establishment of the priority date set forth above, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

4. Applicant's election with traverse of Group II in the reply filed on October 21, 2005 is acknowledged. The traversal is on the grounds that Groups II and III are species of claim 60 and should be separated, if at all, by an election of species rather than restriction. This argument is not found to be persuasive because claim 60 links the inventions of groups II and III and restriction of groups II and III under linking claim restriction practice is proper. Applicant is reminded, as previously set forth that upon allowance of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claim will be entitled to examination. Further, because the method of Group II and the method of Group III involve different method steps and reagents, and thus are materially distinct methods. Therefore, a search for one group would not be coextensive with a search for the other group. The requirement is still deemed proper and is therefore made FINAL.

Specification

5. The specification on page 1 should be amended to reflect the status of the parent application serial number 09/428,156.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the specification should be amended to provide antecedent basis for all of claims 60-77.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 60-65, 67-68 and 74-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 60-65, 67-68 and 74-77 are indefinite in the use of the KSP designation as the sole means for identifying the claimed gene. The use of laboratory designations only to identify a particular gene renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct genes. Amendment of the claims to unambiguously define the recited gene is required.

Claims 60, 62-65, 67, 68, 74-77 are indefinite in that they are incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are determining which comparison result in step (b) results in the assessment of a risk of a hyper-proliferative disorder in step (c).

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 60-65, 67-68 and 74-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to a method of assessing an individual's risk for a hyper-proliferative disorder, particularly cancer, by determining the level of KSP in a sample obtained from the individual and comparing the KSP expression level in the sample with KSP expression level in a control of known proliferation state, and thereby assessing the individual's risk for the hyper-proliferative disorder on the basis of the comparison.

The specification teaches that KSP expression levels can be assessed on a gene or polypeptide level (pages 39, line 35 to page 40, line 1). The specification

teaches that individuals at risk for disease can be treated by the methods of the invention wherein the patients are at risk for restenosis (page 5, lines 5-11).

The teaching of the specification to does not enable one of skill in the art to make and use the invention because the specification does not provide any guidance on differential expression of KSP in individual's at risk for hyper-proliferative disorder compared to control individuals with known proliferation states, does not provide guidance on which hyper-proliferative disorders can be predictably assessed for risk for the hyper-proliferative disease using the instant method. In particular, the specification does not establish a correlation between the level of expression of the KSP gene and the assessment of an individual's risk for a hyper-proliferative disorder. Although drawn to the cancer arts, the teachings of Tockman et al (Cancer Res., 1992, 52:2711s-2718s) are relevant to the instant rejection. Tockman et al. teaches considerations that are necessary in bringing a hyper-proliferative disease biomarker to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Pertinent to the instant rejection, there is no evidence presented in the specification or the art of record that the differential expression, compared to control, of the KSP gene is in any way associated with a hyper-proliferative disorder or that it is a marker for assessing an individual's risk for a hyper-proliferative disorder as claimed. Tockman goes on to teach that markers have clear biological plausibility and **if validated** (emphasis added) can be used for population screening (p. 2713s, col 1). The essential element of the validation of a marker is the ability to test the marker on clinical material obtained from subjects monitored and to link those marker results with subsequent clinical confirmation of, in the instant case, a hyper-proliferative disorder, particularly cancer. This irrefutable link between marker and acknowledged, in this case, hyper-proliferative disorder, is the

essence of a valid marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated (p. 2716s, col 2). Again, the specification does not provide any concrete examples of a correlation between KSP expression levels and an individual's risk a hyper-proliferative disorder, or indicate that any such correlation has been established by experimentation. Given the art recognized necessity to validate disease markers in order to determine if they in fact do what is suggested, and the lack of any concrete examples in the specification, one of ordinary skill in the art would not believe that it is more likely than not that the invention will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

11. Claims 62 and 63 are rejected under 35 USC 112, fourth paragraph as being of improper dependent form for failing to further limit the subject matter of a previous claim. In particular, claims 60, from which claims 62 and 63 depend, is drawn to determining the expression level of KSP in a sample obtained from the individual while claims 62 and 63 broadens claim 60 by requiring the determination of not only the expression level of KSP but also the expression level of a plurality of target molecules correlated with cell proliferation. Further, claim 60 is drawn to comparing the KSP expression level in the sample level to the expression level of KSP in a control of known proliferation state while claims 62 and 63 broaden claim 60 by comparing the expression level of a plurality of target molecules correlated with cell proliferation.

12. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine M. Joyce whose telephone number is 571-272-3321. The examiner can normally be reached on Monday thru Friday, 10:15 - 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Catherine Joyce
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER